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120. A seed of the transgenic plant according to claim 83.

REMARKS

The Amendments

Applicants have replaced the abstract to make it one paragraph.

Support for the abstract is found throughout the specification.

Applicants have added claims 74 to 120. Support for claim 74 may be found throughout the specification. *See, e.g.*, page 3, lines 6-8, page 6, lines 20-25, page 7, lines 27-33 and page 8, lines 20-25. Support for claims 75, 76 and 80 may be found throughout the specification and in originally-filed claim 17. Support for claims 77 and 78 may be found at page 6, lines 32-34 and originally-filed claims 18-19.

Support for claim 79 may be found at page 3, lines 6-8, page 6, lines 20-25 and page 8, lines 12-13. Support for claim 81 may be found throughout the specification and in originally-filed claim 20. Support for claims 82 and 83 may be found throughout the specification. *See, e.g.*, page 22, lines 11-12 and page 23, lines 23-29.

Support for claims 84-94 may be found throughout the specification and in the originally-filed claims. *See, e.g.*, originally-filed claims 17 and 42-52, and the specification at page 3, lines 6-8, page 7, lines 22-33 and page 8, lines 12-13 and 23-24. Support for claims 95-97 may be found in, *e.g.*, originally-filed claims 1, 17 and 56 and the specification at page 22, lines 11-12 and page 23, lines 23-29. Support for claims 98 and 99 may be found throughout the specification. *See, e.g.*, originally-filed claim 58 and page 3, lines 6-8, page 4, lines 27-31, page 9, line 1, and page 21, lines 32-36 of the specification.

Support for claim 100 may be found throughout the specification. *See, e.g.,* originally-filed claim 1 and page 5, lines 18-22 and page 8, lines 9-13. Support for claim 101 may be found in originally-filed claim 5 and in the specification at page 10, lines 8-16 and page 12, lines 6-12. Support for claims 102-103 may be found in originally-filed claims 6-7. Support for claim 104 may be found throughout the specification. *See, e.g.,* page 6, lines 18-25. Support for claims 105-110 may be found. *inter alia*, at page 7, lines 27-33. Support for claims 111, 119 and 120 may be found in originally-filed claim 14.

Support for claims 112-114 may be found throughout the specification. *See, e.g.,* originally-filed claims 21-23, respectively, in originally-filed claims 24-26 and at page 3, lines 6-8 and page 8, lines 9-13 in the specification. Support for claim 115 may be found, *inter alia*, in originally-filed claim 25. Support for claim 116 and 117 may be found throughout the specification. *See, e.g.,* originally-filed claims 27-28 and page 8, lines 20-25. Support for claim 118 may be found throughout the specification. *See, e.g.,* page 23, lines 23-29.

None of the amendments add new matter. Their entry is requested.

Claims 71 and 74-120 are now pending.

Request for Vacating January 10, 2000 Office Action

The Examiner did not examine claims 46, 60 and 63, even though these claims are directed to the invention of Group I and are directed to Species VI, DNA encoding citrate synthase of *S. tuberosum* in antisense orientation. The Examiner admitted that claims 46 and 60 were part of Group I, Species VI (*see* the June 7, 1999

Office Action, pages 2 and 5). Further, applicants pointed out that claim 63, added in the October 7, 1999 Reply to Office Action, also corresponded to Group I, Species VI. See the October 7, 1999 Reply, page 18. SEQ ID NO: 2, recited in claims 46, 60 and 63, is the amino acid sequence of citrate synthase from *S. tuberosum*. Thus, a DNA sequence that encodes SEQ ID NO: 2 is properly part of Group I, Species VI. Added claims 88, 105 and 117 correspond to cancelled claims 40, 63 and 60, respectively. Therefore, applicants request that the January 10, 2000 Office Action be vacated and reissued with an examination of these claims.

The Restriction Requirement

The Examiner states that the response filed October 12, 1999 to the June 7, 1999 restriction requirement is unpersuasive. Specifically, the Examiner admits that the searches for Groups I, III and IV may be expected to overlap but that there is no reason to believe that the searches would be coextensive. The Examiner states that the focus of invention I is to inhibit flower formation whereas the focus of invention III is to improve storage capability. The Examiner states that applicants have not demonstrated that in searching for a transgenic plant of invention I the entire search for storage organs having improved storage capability would be performed. The Examiner further admits that each of inventions I, III and IV require reduced citrate synthase activity, but the desired outcome of such reduced activity for each invention is divergent and thus may be properly restricted.

The Examiner states that even though the U.S. Patent Classifications are the same, divergent database searches would be required, and applicants have not

established that a search for one of the delineated species would encompass a search for all the species. The Examiner states that if evidence is uncovered during the search for the elected species that would render one or more of the non-elected species unpatentable, then the species election with regard to those species will be withdrawn. Applicants traverse.

First, contrary to the Examiner's assertion, a search does not have to be completely coextensive in order not to be a search burden for the Examiner. The Examiner admits that the search overlaps for the inventions of Groups I, III and IV. As discussed previously, a storage organ of a plant is part of the plant. Thus, a search for the transgenic plant of Group I would overlap extensively with the storage organ of the transgenic plant claimed in Group III. Further, the processes of Groups I, III and IV recite the same method steps as each other. *See, e.g.*, claims 112-116. In fact, the Examiner admits that inventions I, III and IV all require reduced citrate synthase activity. Thus, a search for the process of Group I would overlap extensively with that of Groups III and IV.

Second, applicants have established that a search for the invention of Group I would extensively overlap with those of Groups III and IV for the reasons provided above and in the October 19, 1999 response. In addition, it is not up to the applicants to establish that restriction is not required, rather, it is up to the Examiner to demonstrate that it is.

Third, the Examiner has found claims 71 and 17 allowable. *See* the January 10, 2000 Office Action, pages 10-11. Claims 71 and 17 (now replaced as claim 76) are drawn to a recombinant DNA molecule and vector, respectively,

comprising a promoter functional in plants and a DNA sequence coding for citrate synthase, wherein the DNA sequence is fused to the promoter in antisense orientation. These claims are generic. Therefore, at the very least, all species claims that recite DNA molecules and vectors having these elements should be examined. *See* MPEP § 806.04(h) and 37 C.F.R. § 1.141(a), which states that if an application includes an allowable generic claim, then a reasonable number of species may be claimed as well. Claims 74-75, 77-78 and 80-83 depend from either or both claims 71 and 74, and thus should be examined.

Therefore, applicants request that the Examiner withdraw the restriction/election requirement for the reasons provided above.

The Information Disclosure Statement

The Examiner states that an initialed copy of Form PTO-1449 is attached. However, applicants have not received a copy and note that the Form PTO-326 does not indicate that a copy of the PTO-1449 was attached. Applicants request that the Examiner please send the initialed copy of the PTO-1449 with the next communication.

The Drawings

The drawings have been objected to by the Draftsperson for reasons provided in the Notice of Draftsperson's Patent Drawing Review. Applicants stand ready to provide corrected final drawings upon allowance of the present application.

The Specification

The Examiner has objected to the specification because it is not written in a single paragraph format and requires correction.

Applicants have provided herewith a corrected abstract. Withdrawal of this objection to the specification is requested.

The Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1-3, 5, 18, 20, 21, 24, 28, 39, 43, 49, 52, 56-58, 61, 62, 66, 69, 70, 72 and 73 under 35 U.S.C. § 112, second paragraph. The Examiner states that the claims fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse.

As discussed above, applicants have cancelled claims 1-14, 16-24, 28-39, 41, 43-70 and 72-73 and added claims 74-120. Applicants will address these rejections in the context of these added claims 74-120.

The Examiner states that the term "reduced" or "reducing" in claim 1 is a relative term lacking a comparative basis. The Examiner also states that it is unclear what is meant by "displaying inhibition of flower formation."

Claim 1 recited "a reduced citrate synthase activity in comparison to wild type cells." Therefore, claim 1 recited a comparative basis for "reduced." Claim 100, which replaced claim 1, recites "a reduced citrate synthase activity in comparison to the citrate synthase activity of wild type plant cells." Therefore, claim 100 recites a comparative basis for "reduced."

The specification defines inhibition of flower formation on page 4, line 33 to page 5, line 16. The specification states, *inter alia*, that inhibiting flower formation means that the transformed plants either no longer develop any flowers, develop fewer flowers than non-transformed plants or develop non-functional, sterile or partially sterile flowers. The specification also states that inhibiting flower formation means that if transformed plants flower, they flower later than non-transformed plants. Thus, claim 100 is definite with respect to the term "inhibition of flower formation."

The Examiner states that it is unclear what is doing the inhibiting in claims 2, 3 and 24.

Pending claims 98-100 and 112-116 recite that the DNA sequence coding for citrate synthase or a part thereof forms transcripts that suppress endogenous citrate synthase activity. Thus, the pending claims define that it is RNA transcripts through which inhibition of the endogenous citrate synthase activity takes place.

The Examiner states that the term "useful" in claim 5 is a relative term lacking a comparative basis.

Pending claim 101 recites particular plants useful in agriculture and plant breeding and thus is definite.

The Examiner states that it is unclear what "(DSM 8880)" refers for in claim 18.

As originally filed, claim 18 was clear because the specification clearly states that DSM 8880 refers to the deposit number of the plasmid PKS-CSa. Claim 18 has been recast as claim 77, which recites that pKS-CSa is deposited as DSM 8880.

The Examiner states that claim 20 is an improper multiple dependent claim. The Examiner also states that it is unclear whether applicants intend to claim a bacterial cell or a vector. The Examiner states that claim 20 and all other claims that depend from nonelected claims must be amended in response to the Office Action, and states that dependent claims should follow, rather than precede the claims from which they depend.

Claim 20 was not an improper multiple dependent claim because it referred back in the alternative only and did not depend from another multiple dependent claim. Applicants note that it is acceptable that the order of claims may change during prosecution and be in conflict with the requirement that dependent claims refer to a preceding claim because the original number of the claims must be preserved during prosecution. *See* MPEP 608.01(n), Section IV and 37 C.F.R. § 1.126. However, to expedite prosecution, applicants have cancelled claims 1-14, 16-24, 28-39, 41, 43-70 and 72-73 and replaced them with claims 74-120.

Claim 20 has been recast as claim 81 to more clearly define that the bacterial cell comprises either a DNA molecule or a vector.

The Examiner asserts that claim 20 (added claim 81) must be amended so that it does not depend from nonelected claim 19. However, as discussed above, claim 78 (former claim 19) is a species of allowed generic claim 71, and should be examined. Thus, claim 81 is not indefinite for depending from nonelected claim 78.

The Examiner states that claim 24 lacks positive method steps.

Applicants have canceled claim 24 and recast its subject matter in claims 112-114, which recite the steps of introducing a DNA molecule into a plant cell and regenerating a transgenic plant from the cell. Thus, claims 112-114 are not indefinite.

The Examiner states that claim 28 is unclear because it is unclear whether "said DNA sequence" is referring to the "recombinant DNA" or the "DNA sequence" in claim 73. The Examiner also states that "essentially identical," "a part of," "a part thereof" and "derived by insertion, deletion or substitution" are unclear. The Examiner states that "a high degree of homology" and "sufficient" are relative terms lacking a comparative basis. The Examiner also states that how an "antisense effect" is defined is unclear. The Examiner also states that the word "gene" should be "genes" for proper antecedent basis.

Applicants have cancelled claim 28 and replaced it with claim 116. It is clear that "said DNA sequence" refers to the DNA sequence encoding citrate synthase as recited in claims 112-114 and not to the recombinant DNA molecule recited therein. Further, claim 116 does not recite "essentially identical," "a part of," "a part thereof," "derived by insertion, deletion or substitution," "high degree of homology" or "antisense effect," thus obviating these aspects of the rejection. Claims 116 and 117 also properly recite the antecedent basis for a "citrate synthase gene."

Claim 116 recites that the DNA sequence may be one that has at least 65% sequence identity with a defined nucleotide sequence. Claim 117 recites a DNA sequence that encodes an amino acid sequence that has at least 65% sequence identity

with a defined amino acid sequence. The recitation of 65% sequence identity is definite because it provides the metes and bounds of the claimed subject matter.

Claims 116 and 117 recite that the DNA sequence exhibits "sufficient sequence identity to an endogenous citrate synthase gene to inhibit expression of said endogenous citrate synthase gene, relative to the expression of said endogenous citrate synthase gene in a wildtype plant cell, when the DNA molecule is introduced and transcribed in a transgenic plant cell." Thus, the term "sufficient sequence identity" is definite because the claim recites that the sequence identity must be at least 65% and must be sufficient to inhibit expression of the endogenous citrate synthase gene. Thus, the DNA sequence is described both structurally and functionally and is adequately defined.

The Examiner states that claim 39 lacks positive steps. Applicants have cancelled claim 39 and thus have obviated this rejection.

The Examiner states that the term "originates" in claim 43 is unclear. Applicants have cancelled claim 43 and replaced it with claim 85, which replaces the term "originates" with "is," thereby obviating this rejection.

The Examiner states that amended claim 49 should be clarified as twice amended. Applicants have cancelled claim 49 and thus have obviated this rejection.

The Examiner states that claim 56 is an improper multiple dependent claim and that it is unclear what applicants intend to claim.

Claim 56 was not an improper multiple dependent claim because it referred back in the alternative only and did not depend from another multiple dependent claim. Further, claim 56 has been recast as claim 95 to more clearly recite

that the bacterial cell comprises a DNA molecule or a vector comprising said DNA molecule.

The Examiner states that claim 58 is unclear what protein is expressed from "expressing from said DNA molecule non-translatable mRNA." The Examiner asserts that "[e]xpression is understood by one skilled in the art to mean protein expression."

Contrary to the Examiner's assertion, the term "expression" or "gene expression" encompasses not only "protein expression" but such processes as transcription, RNA processing and transport, mRNA degradation and protein translation. *See, e.g.,* Alberts et al., Molecular Biology of the Cell, New York: Garland Publishing, Inc. 1983, page 437. Thus, the term "expression" was correctly used in claim 58. Claim 58 has been cancelled and recast as claim 98. To expedite prosecution, claim 98 recites "transcribing" non-translatable RNA from the DNA molecule.

The Examiner states that the EC number should follow "citrate synthase" rather than "family" in claim 61. Applicants have cancelled claim 61 and recast it as claim 84. The EC number follows "citrate synthase" and thereby obviates this rejection.

The Examiner states that claim 73, part (ii) should be amended to recite "transcribed" because "expressed" is understood by one skilled in the art to be related to protein expression.

As discussed above, the term "expressing" encompasses transcription, translation and other mechanisms. However, to expedite prosecution, claims 112-114,

which are based in part on claim 73, recites that the DNA molecules forms transcripts, thereby obviating this rejection.

The Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claim 58 under 35 U.S.C. § 112, first paragraph, for allegedly not being described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner states that amending "mRNA" to "RNA" broadens the scope of the claim. Applicants traverse.

Claim 58 has been cancelled and recast as added claims 98 and 99, which recite "non-translatable mRNA," thereby obviating this rejection.

The Examiner has rejected claim 18 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Specifically, the Examiner states that it is unclear whether the claimed plasmid pKS-CSa (DSM 8880) is readily available to the public or easily reproducible to one skilled in the art. If not, the Examiner states that a deposit of said plasmid necessary to practice the claimed invention and in compliance with 37 C.F.R. §§ 1.801-1.809 is required. Applicants traverse.

Applicants submit herewith a statement by the undersigned declaring that the plasmid PKS-CSa was deposited under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the

deposited material will be irrevocably removed upon the granting of a patent.

Therefore, applicants have obviated this rejection for claims 77 and 78.

The Examiner has rejected claims 1-3, 5, 18, 20, 21, 24, 28, 39, 43, 49, 52, 56-58, 61, 62, 66, 69, 70, 72 and 73 under 35 U.S.C. § 112, first paragraph. The Examiner states that the specification enables the use of antisense RNA of SEQ ID NO: 1 or a nucleotide sequence encoding citrate synthase. However, the Examiner states that the specification does not teach methods other than the use of antisense RNA for reducing citrate synthase activity and thus does not reasonably provide enablement for any method of inhibiting flower formation by reducing citrate synthase activity. Applicants traverse.

As discussed above, applicants have cancelled claims 1-14, 16-24, 28-39, 41, 43-70 and 72-73 and added claims 74-120. Applicants will address these rejections in the context of these added claims 74-120.

The Examiner states that claim 1 reads on transgenic plants with reduced citrate synthase due to undisclosed mechanisms because there is no relationship between the plants being transgenic and having reduced citrate synthase activity. The Examiner asserts that, with respect to claim 39, applicants do not teach how a DNA molecule that codes for citrate synthase should be used to inhibit flower formation. The Examiner also states that it is unclear what antisense RNA other than that of the citrate synthase gene could be used to inhibit endogenous citrate synthase expression without further guidance and undue experimentation.

Claim 1 has been cancelled and recast as claim 100. Claim 100 recites a transgenic plant comprising transgenic plant cells which contain a DNA molecule

comprising a promoter functional in plants and a DNA sequence encoding citrate synthase or a part thereof of at least 15 basepairs. Claim 100 also recites that transcription of the DNA molecule suppresses an endogenous citrate synthase activity. Thus, claim 100 recites a relationship between a plant being transgenic and a reduction in citrate synthase activity. In fact, all of the pending claims recite the relationship between the expression of a DNA molecule encoding citrate synthase or a part thereof and the reduction of expression of an endogenous citrate synthase gene. Therefore, applicants have obviated the Examiner's rejection regarding using a gene other than that of citrate synthase to inhibit citrate synthase expression.

The Examiner states that other than using the antisense sequence for citrate synthase, it is unpredictable to determine what mechanisms would inhibit or reduce citrate synthase activity or expression of endogenous DNA sequences. The Examiner asserts that it is unclear how a coding region of a citrate synthase gene operably linked to a promoter and transcribed into mRNA would suppress the activity of endogenous citrate synthase and inhibit flower formation. The Examiner states that the applicants do not teach that an increased level of citrate synthase in a cell would suppress the activity of endogenous citrate synthase.

Claims 71-83, 104-111 and 115-120 are drawn to the use of antisense RNA complementary to a DNA molecule encoding citrate synthase. Thus, these claims are enabled by the specification, as admitted by the Examiner. Further, contrary to the Examiner's assertions, the prior art teaches that expression of an increased level of a gene transcript can suppress the level of an endogenous protein through a process that is often called "co-suppression." For instance, United States Patent 5,283,184

(hereafter "the '184 patent") discloses a method of expressing the sense strand of a gene under the operational control of a promoter to suppress the expression of a cellular gene product. *See, e.g.*, col. 3, lines 7-35 and 54-66 of the '184 patent. The '184 patent was issued prior to the priority date of the instant application. Thus, the method of co-suppression was known in the art at the time the invention was made.

The instant application states that the DNA sequences encoding citrate synthases, such as those from the *Solanaceae* and *Chenopodiaceae* family, may be integrated into the plant genome to "permit the formation of transcripts by which an endogenous citrate synthase activity can be suppressed." *See, e.g.*, page 3, lines 14-21. *See also* page 5, lines 18-28. "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information *known in the art* without undue experimentation." *United States v. Telectronics, Inc.*, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988, emphasis added). "A patent need not teach, and preferably omits, what is well known in the art." *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986). *See* MPEP 2164.01. Thus, given the teachings in the specification combined with what was known in the prior art regarding co-suppression of gene expression in plants, the instant application enables the use of a citrate synthase gene transcribed in sense orientation to suppress the endogenous citrate synthase gene.

The Examiner states that, with regard to claim 58, there is no evidence that the synthesis of endogenous citrate synthase is prevented, that plants do not require citrate synthase, and that non-translatable RNA would be able to block all synthesis of endogenous citrate synthase.

Claim 58 has been recast as claims 98 and 99. Claims 98 and 99 recite a method of reducing the synthesis of citrate synthase by introducing a DNA molecule encoding citrate synthase into a cell and transcribing non-translatable mRNA from said DNA molecule, wherein said transcribing results in a reduction in the synthesis of endogenous citrate synthase in the transgenic plant cell. The specification exemplifies a method of reducing citrate synthase synthesis by introducing a DNA molecule encoding citrate synthase into a cell. *See, e.g.*, Fig. 7 and page 28, lines 9-14. Thus, the specification provides guidance for the practice of claims 98 and 99.

The Examiner states that Landschuetze et al., EMBO J. 14: 660-666, 1994 (hereafter "Landschuetze") discloses transgenic potato plants that express antisense RNA and that have a strong reduction in citrate synthase activity. The Examiner states that although flower buds formed at least two weeks later than wild type plants and the flower buds were aborted at an early stage of development, there was still flower formation. The Examiner states that the applicants have provided no guidance as to what other method would reduce citrate synthase by at least 30% resulting in inhibition of flower maturation.

As discussed above in response to the rejection of claim 1 under 35 U.S.C. § 112, second paragraph, with respect to "inhibition of flower formation," the specification defines inhibition of flower formation on page 4, line 33 to page 5, line 16 to include, *inter alia*, delayed and/or aborted flowering. Thus, Landschuetze fully supports the enablement of the claimed invention.

The Examiner states that, with reference to claim 28, it is an invitation to experiment requiring undue experimentation for one skilled in the art to determine

what part of SEQ ID NO: 1 or which insertion/deletion/substitution of SEQ ID NO: 1 would elicit an "antisense effect" without further guidance as to how inoperable embodiments can be predictably and reliably eliminated without undue experimentation. The Examiner also states that a coding region could be as little as a single codon, which the Examiner states is unlikely to work based upon the state of the prior art. The Examiner also states that a DNA sequence complementary to the citrate synthase gene, as recited in claim 73, reads on a two-nucleotide sequence, which the Examiner states is unlikely to work based upon the state of the prior art and applicants' lack of evidence to the contrary.

Applicants have cancelled claim 28 and replaced it with claim 116. Claim 116 recites that the DNA sequence must have at least 65% sequence identity to one of the specified sequences encoding citrate synthase and must exhibit sufficient sequence identity to an endogenous citrate synthase gene to reduce expression of the endogenous gene. Further, claims 112 to 114, from which claim 116 depends, recite that the DNA sequence coding for citrate synthase or a part thereof must be at least 15 basepairs and sufficient in length to suppress endogenous citrate synthase activity. Thus, claim 116 requires that the DNA sequence must be at least 15 basepairs in length, have at least 65% sequence identity to a specified sequence encoding citrate synthase and must be able to inhibit expression of the endogenous citrate synthase gene. Similarly, claims 79, 84, 100 and the claims that depend therefrom recite that the DNA sequence coding for citrate synthase or part thereof must be at least 15 basepairs and able to suppress endogenous citrate synthase activity. Thus, none of claims 71 and 74-120 encompass a DNA sequence of only two nucleotides or a single codon.

The specification discloses that partial sequences of at least 15 basepairs and sequences with at least 65% sequence identity to a citrate synthase gene may be used to inhibit endogenous citrate synthase activity. *See, e.g.*, page 8, lines 12-25. The specification also teaches that these DNA sequences can be used in processes for inhibiting flower formation and making transgenic plants in a wide variety of different plant species, including potato, tobacco and sugar beet. *See, e.g.*, page 9, line 35 to page 10, line 25. The specification discloses methods of introducing the DNA sequences into a plant. *See* page 21, lines 32 to page 23, line 29 and page 31, line 5 to page 32, line 32. The specification also discloses methods of determining the citrate synthase activity and mRNA levels in a transgenic plant cell or transgenic plant. *See* page 33, line 1 to page 34, line 17. Thus, contrary to the Examiner's assertions, it would not require undue experimentation to determine whether a particular DNA sequence inhibits the endogenous citrate synthase activity in a transgenic plant cell. Rather, it would require only routine experimentation, using methods provided in the specification or known to one of ordinary skill in the art, to determine whether a specific DNA sequence inhibits endogenous citrate synthase activity.

Conclusion

For the reasons presented above, applicants request allowance of claims

7 and 74-120.

Respectfully submitted,

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